

In the Specification:

Page 23, line 13, as shown;

Page 25, lines 14, 22, 27, and 27 respectively, as shown; and

Page 45, line 9, as shown.

In the Drawing:

Inclusion of a copy of Fig. 9, as previously submitted; and

Amended Fig. 10, as shown.

In the Claims:

Cancel claims 1-10 respectively, without prejudice; and

Amend pending claims 11-15 respectively, as shown.

In accordance with the particular requirements of 37 C.F.R.121, paragraphs (b) through (d), the following documents are individually enclosed: A marked-up version of the present amendments to the Specification; a clean copy version of the present amendments to the Specification; a marked-up version of the present amendments to the claims; and substitute pages for Figs. 9 and 10 respectively.

In addition, in view of the explicit holdings rendered by the U.S. Supreme Court in the *Festo* case recently decided on May 28, 2002 [*Festo Corp. v. Shoketsu Kinzoku Kabushiki Co. Ltd. et al.*, 62 U.S.P.Q.2d 1705

(2002)] concerning the applicability of the legal doctrine of equivalents to amended claim language, applicants now present a formal attestation and affirmation of their legal position and substantive rights: Applicants do not now surrender for any reason, nor have previously surrendered at any time or for any reason during the prosecution of the instant application, any inventive subject matter which is or could be expected to be a particular equivalent of the invention defined by the language of the amended claims then pending by a person ordinarily skilled in this art; and that no presumption of estoppel, either in law or equity, exists or pertains now or at any time previously as a potential bar to the application of the doctrine of equivalence for any and all possible embodiments which may be found to be encompassed now or in the future by the language of the amended claims proffered now or at any time previously for examination to the U.S. Patent Office. Accordingly, applicants affirmatively rebut and explicitly dispute any presumption that the doctrine of equivalence for the language of the amended claims has been surrendered or is not in full force for any reason and at any time during the prosecution for any and all amended claims prosecuted for the instant application.

Accordingly, the language of pending amended claims 11-15 respectively is now offered in clear copy format for review under the

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circumstances stated above, as follows:

11 (Thrice Amended). A PR-39 derived oligopeptide family whose members individually cause a selective inhibition of proteasome-mediated degradation of at least one specific peptide in-situ after introduction intracellularly to a viable cell, each member of said PR-39 derived oligopeptide family being

less than 26 amino acid residues in length;

an oligopeptide whose N-terminal amino acid residue sequence begins with Arg-Arg-Arg;

an analog of the amino acid sequence of native PR-39 peptide;

pharmacologically active for altering the proteolytic degradation activity of proteasomes in-situ;

able to interact in-situ with at least the  $\alpha_7$  subunit of such proteasomes as are present within the cytoplasm of the cell; and

able selectively to alter the proteolytic degradation activity of said proteasomes having an interacting  $\alpha_7$  subunit such that the proteolytic degradation mediated by said proteasomes against at least one specific peptide becomes inhibited while the proteolytic degradation mediated by said proteasomes against other peptides remains unaltered.

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12 (Thrice Amended). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 15 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg-Pro-Arg-Pro-Pro (SEQ ID NO: 3).

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13 (Thrice Amended). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 11 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg (SEQ ID NO: 4).

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14 (Thrice Amended). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 8 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr (SEQ ID NO: 5).

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15 (Twice Amended). A PR-39 derived oligopeptide family whose members cause a selective inhibition of protease-mediated degradation of at least one specific peptide in-situ after introduction intracellularly to a viable cell, each member of said oligopeptide family being:

less than 20 amino acid residues in length;  
an oligopeptide whose N-terminal amino acid residue sequence begins with Arg-Arg-Arg;

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*Conclude*

an analog of the amino acid sequence of native PR-39 peptide;  
pharmacologically active for altering the proteolytic degradation  
activity of proteasomes in-situ;  
able to interact in-situ with at least the  $\alpha_7$  subunit of such  
proteasomes as are present within the cytoplasm of the cell; and  
able selectively to alter the proteolytic degradation activity of  
said proteasomes having an interacting  $\alpha_7$  subunit such that the  
proteolytic degradation mediated by said proteasomes against at least one  
specific peptide becomes inhibited while the proteolytic degradation  
mediated by said proteasomes against other peptides remains unaltered.

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